

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (currently amended) An apparatus for performing the polymerase chain reaction in a plurality of liquid reaction mixtures, said apparatus including a plurality of vials containing such liquid reaction mixtures, said vials having an upper portion and a lower portion, said apparatus comprising:

an assembly for cycling said vials through a series of temperature excursions;

a cover for applying a seating force to said vials and for applying a constant temperature to the upper portion of said vials; and

CI a computing apparatus for controlling said temperature excursions of said assembly and said constant temperature of said cover;

said assembly including:

a sample block for receiving said vials;

a plurality of thermoelectric devices controlled by said computing apparatus;

a heat sink;

a clamping mechanism positioned so as to clamp said thermoelectric devices between said sample block and heatsink;

a heater positioned around the perimeter of said sample block; and

a pin having a first end and a second end, said first end in close contact with said sample block and said second end in close contact with said heatsink so as to provide a thermal path between said sample block and said ~~heatsink~~ heatsink, said pin being positioned to reduce thermal gradients across said sample block.

2. (canceled)

3. (previously presented) The apparatus of claim 1 wherein said sample block comprises:
a plurality of sample wells, for receiving sample vials, each well having a top and
bottom;

an upper support plate connecting the tops of said sample wells; and
a bottom plate connecting the bottoms of said sample wells.

4. (original) The apparatus of claim 3 wherein said upper support plate and said sample
wells are electroformed as a single piece.

5. (original) The apparatus of claim 3 wherein said sample block is comprised of silver.

C1 6. (original) The apparatus of claim 3 wherein said sample wells are arranged in an 8 x 12
array.

7. (original) The apparatus of claim 3 wherein said sample block is rectangular.

8. (previously presented) The apparatus of claim 1 wherein said thermoelectric devices
are matched to provide a temperature within 0.2 C for a given input current.

9. (previously presented) The apparatus of claim 1 wherein said thermoelectric devices
comprise:

a first ceramic layer having bonded copper traces;

a second ceramic layer having bonded copper traces, said second ceramic layer
comprising a plurality of ceramic elements; and

a plurality of bismuth telluride pellets positioned between said first ceramic layer and said second ceramic layer and soldered to said bonded copper traces on said first and second ceramic layers.

10. (original) The apparatus of claim 9 wherein the ceramic of said first and second layer is alumina.

11. (original) the apparatus of claim 9 wherein the ceramic layers have a thickness of 0.508mm.

12. (original) The apparatus of claim 9 wherein said bismuth telluride pellets are soldered using high temperature solder.

13. (previously presented) The apparatus of claim 9 wherein electrical resistance of the devices is determined from the equation:

$$R=nr(h/A)$$

wherein R is the electrical resistance of the device, n is a number equal to how many pellets are in the device, r is resistivity of the bismuth telluride being used in the pellets, h is height of the pellets and A is cross sectional area of the pellets.

14. (previously presented) The apparatus of claim 1 wherein said heatsink comprises:
a plate having a top side and a bottom side;
a plurality of fins extending perpendicularly from said bottom side;
a trench extending around the perimeter of said top side to impede heat loss from said perimeter;
a fan placed in close proximity to said fins to control air flow through said fins; and

a recess within said plate for receiving a temperature sensor.

15. (currently amended) The ~~assembly~~ apparatus of claim 1 wherein said clamping mechanism comprises:

a ~~spine and spine~~, said spine having a plurality of openings in said spine for receiving fasteners; and
a plurality of fingers extending laterally from said spine.

16. (currently amended) The apparatus ~~mechanism~~ of claim 15 wherein said spine is rectangular in shape.

17. (currently amended) The apparatus ~~mechanism~~ of claim 15 wherein said fingers are rectangular in shape.

d 18. (original) The apparatus of claim 15 wherein said fingers have a top and a bottom and are tapered so as to have less width at said top than at said bottom.

19. (original) The apparatus of claim 15 wherein said fingers have a first end protruding laterally from said spine and a protrusion extending downward from said first end.

20. (original) The apparatus of claim 15 wherein said fingers have a beveled front edge.

21. (original) The apparatus of claim 15 wherein each of said openings are located in close proximity to a corresponding finger.

22. (previously presented) The apparatus of claim 1 wherein said heater comprises an electrically resistive path embedded in a frame shaped film carrier.

23. (currently amended) The apparatus of claim 22 wherein said electrically resistive path comprises a first set of sections located on opposite sides of said frame shaped carrier having a first power density and a second set of sections located on opposite sides of said frame shaped carrier having a second power density.

24. (previously presented) The apparatus of claim 1 further comprising an associated memory device capable of storing data related to said assembly.

25. (previously presented) The apparatus of claim 1 wherein said cover comprises:
a platen, vertically and horizontally displaceable in relationship to said vials, said platen including:

CI an array of openings corresponding to locations of said vials, said openings having a perimeter corresponding to a perimeter of said vials;

a skirt extending downward around the perimeter of said platen, said skirt having dimensions corresponding to the perimeter of a standard microtiter tray, said skirt constructed to engage said perimeter of said tray during vertical displacement of said platen, causing said openings in said platen to engage said perimeter of said vials, applying a seating force on said vials for maintaining a snug fit between walls of said sample vials and said assembly for receiving said sample vials;

means for forcibly lowering said platen to maintain said seating force; and

heating means positioned in close contact with said platen to maintain said platen at a constant temperature.

26. (previously presented) The apparatus of claim 1 wherein said assembly comprises at least one device for changing the temperature of said apparatus, further comprising a system for measuring the AC resistance of said thermoelectric device.

27. (previously presented) The apparatus of claim 26 wherein at least one device has a first heating and cooling surface and a second heating and cooling surface, said system comprising:

a first temperature sensor positioned so as to be in thermal communication with said first heating and cooling surface;

a second temperature sensor positioned so as to be in thermal communication with said second heating and cooling surface;

a bi-polar amplifier circuit for providing power to said thermoelectric device;

a circuit for sensing AC voltage across said thermoelectric device and producing a DC voltage representing said AC voltage;

a circuit for sensing AC current through said thermoelectric device and producing a DC voltage representing said AC current;

a microcontroller programmed to receive said signals from said first and second temperature sensors;

said microcontroller further programmed to cause said bi-polar amplifier to provide power to said thermoelectric device so that said first and second temperature sensor signals indicate equal temperatures;

said microcontroller further programmed to cause an AC voltage to be superimposed on said bi-polar amplifier power;

said microcontroller further programmed to receive said voltages produced by said circuit for sensing AC voltage and from said circuit for sensing AC current;

said microcontroller further programmed to calculate the AC resistance of said thermoelectric device from said voltages;

said microcontroller further programmed to compensate for ambient temperature error by performing a polynomial calculation; and

said microcontroller further programmed to store said compensated AC resistance measurement.

28. (previously presented) A method for measuring the AC resistance of a thermoelectric device having a first heating and cooling surface and a second heating and cooling surface, said method comprising;

- measuring the temperature of said first heating and cooling surface;
- measuring the temperature of said second heating and cooling surface;
- applying power to said thermoelectric device to cause said first heating and cooling surface and said second heating and cooling surface to attain the same temperature;
- applying an AC voltage across said thermoelectric device;
- measuring said AC voltage across said thermoelectric device;
- measuring AC current through said thermoelectric device;
- calculating the AC resistance of said thermoelectric device from said measured AC voltage and said measured AC current.

C1 29. (original) The method of claim 28, further comprising:

- performing a calculation for compensating for ambient temperature error to calculate a compensation AC resistance measurement; and
- storing said compensated AC resistance measurement.

30. (previously presented) A method for achieving linear temperature transitions utilizing a thermoelectric device having a Seebeck coefficient, at least a first heating and cooling surface and a second heating and cooling surface and being operated in a manner causing said first surface to be higher in temperature and said second surface to be lower in temperature relative to each other; said method comprising:

- determining a desired heat flow from said lower temperature surface;
- determining electrical resistance of said thermoelectric device as a function of temperature;
- determining the Seebeck coefficient of said thermoelectric device as a function of temperature;

determining conductance of said thermoelectric device as a function of temperature;
measuring temperature of said lower temperature surface;
measuring temperature of said higher temperature surface;
calculating an average temperature of said lower temperature surface and said higher temperature surface; and

calculating a current required to achieve said desired heat flow as a function of said electrical resistance of said thermoelectric device as a function of temperature, said Seebeck coefficient of said thermoelectric device as a function of temperature, said conductance of said thermoelectric device as a function of temperature, said temperature of said lower temperature surface, said temperature of said higher temperature surface, and said average of said lower temperature surface and said higher temperature surface.

C 31. (previously presented) A method for determining the temperature of a mixture in a sample vial, said vial having an upper portion and a lower portion and being contained in an apparatus including:

an assembly for cycling said vials through a series of temperature excursions, said assembly further comprising a sample block for receiving said vials;

a cover for applying a seating force on said vials and for applying a constant temperature to the upper portion of said vials; and

a computing apparatus for controlling said temperature excursions of said assembly and said constant temperature of said cover;

said method comprising:

measuring temperature of said sample block;

measuring temperature applied by said cover;

determining thermal resistance of said vial between said sample block and said mixture;

determining thermal resistance for air in parallel with said vial between said mixture and said cover;

determining thermal capacitance of said mixture;

determining thermal capacitance of said vial between said mixture and said cover; and
calculating temperature of said mixture as a function of said temperature of said sample
block, said temperature applied by said cover, said thermal resistance of said vial between said
sample block and said mixture, said thermal resistance of air in parallel with said vial between
said mixture and said cover, said thermal capacitance of said mixture and said thermal
capacitance of said vial between said mixture and said cover.

32. (currently amended) A method of calibrating an assembly for cycling samples
through a series of temperature excursions comprising a sample block for receiving vials, a
plurality of ~~thermal-electric~~ thermoelectric devices, a heat sink, a clamping mechanism
positioned so as to clamp said ~~thermal-electric~~ thermoelectric devices between said sample block
and said heatsink, and a memory device capable of storing data related to said assembly, said
method comprising:

C1 applying power to said ~~thermal-electric~~ thermoelectric devices, causing said assembly to
cycle through a desired series of temperature excursions;

measuring the actual temperature excursions;

comparing said actual temperature excursions with said desired temperature excursions;

adjusting said power applied to said ~~thermal-electric~~ thermoelectric devices so that said
actual temperature excursions match said desired temperature excursions; and

recording said adjusted power in said memory device located on said assembly for further
utilization in obtaining said desired series of temperature excursions.

33. (currently amended) An assembly for cycling vials of reaction mixtures through a
series of temperature excursions, comprising:

a sample block for receiving vials of reaction mixtures;

a plurality of thermoelectric devices;

a heat sink;

a clamping mechanism positioned so as to clamp said thermoelectric devices between said sample block and said heatsink;

a heater positioned around a perimeter of said sample block;

a pin having a first end and a second end, said first end in close contact with said sample block and said second end in close contact with said heatsink so as to provide a thermal path between said sample block and said ~~heatsink; and heatsink~~, said pin being positioned to reduce thermal gradients across said sample block; and

means for connecting the assembly to a power source for said heater and a computing apparatus for controlling said temperature excursions of said assembly and said heater.

C1 34.-43. (canceled)

44. (previously presented) The assembly of claim 33, wherein said pin is positioned at the center of the sample block.

C2 45. (new) The apparatus of claim 1, wherein said pin is positioned at the center of the sample block.